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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/087,466

03/01/2002

Alexander Olek

81659A

6657

7590

03/25/2005

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EXAMINER

MAHATAN, CHANNING

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/087,466

Applicant(s)

OLEK ET AL.

Examiner

Channing S. Mahatan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 November 2004.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 and 41 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-36 and 41 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

APPLICANTS' ELECTION

Applicants' election of Group I (claims 1-36 and 41; drawn to a method and device for the development/generation of gene panels) in the reply filed on 01 November 2004 is acknowledged. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)).

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 1-36 and 41. Claims 37-40 and 42-58 have been canceled.

Claims Rejected Under 35 U.S.C. § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-36 and 41 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

VAGUE AND INDEFINITE

Claims 1, 31, and all claims dependent therefrom recite the limitation "methylation relevant regions" which is considered vague and indefinite. The specification indicates the following with respect to "methylation relevant regions":

"According to the invention it is further preferred to analyse methylation relevant regions comprising the complete genes and/or promoters, introns, first exons and/or enhancers of the genes to be analysed. From the analysis of the methylation sites which are relevant for the expression of a certain gene, but not localised inside the sequence of the gene itself, the effect of

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the site for the expression of the gene can be readily extrapolated by the person skilled in the art.”
(page 26, lines 4-11)

However, it is unclear from the specification and the cited portion above what Applicants’ regard “relevant” to encompass when applied to “methylation regions”. For instance, what criteria(s) or parameters distinguish “methylation regions” to be considered relevant versus irrelevant? Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 1 and all claims dependent therefrom recite the limitation “wherein the gene is selected on the basis of the first knowledge base” which is considered vague and indefinite. The language “selected on the basis” implies some set of features for the gene to be selected, which is unclear. It is therefore unclear what features, per se, of the “first knowledge base” is utilized for gene selection. Clarification of the metes and bounds, via clearer claim language, is requested.

Regarding claims 9, 21, and 36, the phrase “for example” renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See M.P.E.P. § 2173.05(d). Clarification of the metes and bounds, via clearer claim language, is requested.

Regarding claims 16 and 27, the phrase “such as” renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See M.P.E.P. § 2173.05(d). Clarification of the metes and bounds, via clearer claim language, is requested.

LACK OF ANTECEDENT BASIS

Claims 13 and 24 recite the limitation “the selection is based on the result of at least two individual rows of analyses” which appears to lack proper antecedent basis. While it is acknowledged claim 1 indicates the steps of “analysing” and “selecting”, the instant claim fails

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to provide any indication of “at least two individual rows” in these steps. Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 34 recites the “the identical biological material, different biological material or combination thereof is used in step a)” which lacks proper antecedent basis. Claim 1 step a) recites “isolating at least one biological sample from each of at least two groups of biological material containing mRNA and/or protein”. However, claim 1 (which claim 34 depends from) fails to denote the utilization of “identical biological material, different biological material or combination thereof”. Rather claim 1 utilizes “two groups of biological material containing mRNA and/or protein” and fails to provide any further provisos.

Claims Rejected Under 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-8, 19, and 20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Huang et al. (Methylation profiling of CpG islands in human breast cancer cells. Human Molecular Genetics. 1999, Volume 8, Number 3, pages 459-470) taken in view of Duggan et al. (Expression profiling using cDNA microarrays. Nature Genetics. January 1999, Volume 21, Number 1, pages 10-14).

Huang et al. describes a novel array-based method (DMH) that allows for a genome-wide screening of hypermethylated CpG islands in tumor cells (Abstract). Utilizing different isolated breast cancer cell lines (instant claim 1 step “a)” and instant claims 2-5) the authors detect and

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select (instant claim 1 steps “b)-c)”) for the mRNA expression level of DNMT1 and p21 (instant claim 6) by Northern Blot analysis (instant claims 7-8) (page 460, left column, lines 26-49; and Figure 1). The authors then proceed to determine the extent of CpG island sequences (i.e. cytosine methylation; instant claims 1 step “d)” and instant claim 19) undergoing de novo methylation in the six cancer cell lines utilizing MseI enzyme (instant claim 20)(page 460, left column, lines 52-56; and Figure 2). CpG island clones were then selected and gridded on high-density arrays (instant claim 1 steps “e)-f)” and instant claim 35; pages 460-461, beginning on the right column, line 21). However, Huang et al. does not specifically state the utilization of a database for storing obtained data for the construction of the array.

Duggan et al. reviews the technical aspects of cDNA microarrays, including the general principles of fabrication of the arrays, target labeling, image analysis and data extraction, management and mining (Abstract). The authors state “All array methods require the construction of databases for the management of information on the genes represented on the array...” (instant claim 1 generating a...“knowledge base”; page 13, right column, lines 30-32).

EXAMINER COMMENT

Regarding the limitation “knowledge base” the specification provides the following:

“...the knowledge base will comprise only “on” and “off” type of data which allows for a very simple decision between expressed or non-expressed genes.” (page 25, lines 4-6)

Therefore, the limitation “knowledge base”, in view of the above, is interpreted to refer to a database of “on” and “off”, per se, gene expression data.

DUPLICATE CLAIM WARNING

Applicants are advised that should claims 13, 16, 17, and 18 be found allowable, claims 24, 27, 28, 29, and 36 will be objected to under 37 C.F.R. § 1.75 as being a substantial duplicate

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thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See M.P.E.P. § 706.03(k).

OBJECTION TO DISCLOSURE

The disclosure is objected for the following reasons:

The specification contains several instances (page 2, lines 18 & 19; page 3, lines 10 & 14, and throughout the remainder of the specification) where the format of the first quotation is located incorrectly. For example, referring to page 2, line 18 the following format appears:

“„Proteomics....”

This appears inconsistent with general utilization of quotations. Appropriate correction is requested.

The specification contains a grammatical error on page 37, line 14; wherein “2-D Gelelectrophoresis” should be replaced with “2-D Gel electrophoresis”. Appropriate correction is requested.

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either 571-273-8300.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is (571) 272-0717. The Examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify Applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables Applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Examiner Initials: *CSM*

Date: *March 4, 2005*

Ardin H. Marschel 3/17/05
ARDIN H. MARSCHEL
PRIMARY EXAMINER